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=> d his

     (FILE 'HOME' ENTERED AT 15:44:50 ON 06 JUL 2005)

     FILE 'HCAPLUS' ENTERED AT 15:45:00 ON 06 JUL 2005
L1            1 US20040224951/PN OR US2002-403037#/AP,PRN

     FILE 'REGISTRY' ENTERED AT 15:45:45 ON 06 JUL 2005

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L2               TRA L1 1- RN :       20 TERMS

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L3            20 SEA L2

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L4            1 US20040224951/PN OR US2002-403037#/AP,PRN

=> b hcap
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FILE COVERS 1907 - 6 Jul 2005  VOL 143 ISS 2
FILE LAST UPDATED: 5 Jul 2005  (20050705/ED)

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 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> d all l1 tot

L1   ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2005 ACS on STN
AN   2004:143163  HCAPLUS
DN   140:175195
ED   Entered STN:  22 Feb 2004
TI   5,6-Fused uracil derivatives as matrix metalloproteinase inhibitors,
     pharmaceutical compositions, and therapeutic use
IN   Roark, William Howard
PA   Warner-Lambert Company LLC, USA
SO   PCT Int. Appl., 193 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
IC   ICM  C07D495-04
     ICS  C07D471-04; A61K031-519; A61P019-02
CC   1-12 (Pharmacology)
     Section cross-reference(s): 63
FAN.CNT 1
     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
PI   WO 2004014921         A1    20040219    WO 2003-IB3505          20030804 <--
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
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CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,
TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004224951 A1 20041111 US 2003-634489 20030805 <--
PRAI US 2002-403037P P 20020813 <--

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2004014921	ICM	C07D495-04
	ICS	C07D471-04; A61K031-519; A61P019-02
WO 2004014921	ECLA	C07D471/04+239B+221B; C07D495/04+335B+239B <--
US 2004224951	NCL	514/242.000; 514/262.100; 514/264.100; 544/184.000; 544/256.000; 544/279.000
	ECLA	C07D471/04+239B+221B; C07D495/04+335B+239B <--

OS MARPAT 140:175195

AB The invention provides 5,6-fused uracil derivs.,or pharmaceutically acceptable salts thereof. The invention also provides pharmaceutical compns. comprising a compound of the invention, or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier, diluent, or excipient. The invention also provides methods of inhibiting a MMP-13 enzyme in an animal, comprising administering a compound of the invention, or a pharmaceutically acceptable salt thereof. The invention also provides methods of treating a disease mediated by an MMP-13 enzyme in a patient, comprising administering to the patient a compound of the invention, or a pharmaceutically acceptable salt thereof, either alone or in a pharmaceutical composition The invention also provides methods of treating diseases such as heart disease, multiple sclerosis, osteo- and rheumatoid arthritis, arthritis other than osteo- or rheumatoid arthritis, cardiac insufficiency, inflammatory bowel disease, heart failure, age-related macular degeneration, chronic obstructive pulmonary disease, asthma, periodontal diseases, psoriasis, atherosclerosis, and osteoporosis in a patient, comprising administering to the patient a compound of the invention, or a pharmaceutically acceptable salt thereof, either alone or in a pharmaceutical composition The invention also provides combinations, comprising a compound of the invention, or a pharmaceutically acceptable salt thereof, together with another pharmaceutically active component.

ST fused uracil deriv matrix metalloproteinase inhibitor therapeutic

IT Drug delivery systems
(capsules; fused uracil derivs. as matrix metalloproteinase inhibitors, pharmaceutical compns., and therapeutic use)

IT Ampuls
Antiarthritics
Arthritis
Drug delivery systems
Human
(fused uracil derivs. as matrix metalloproteinase inhibitors, pharmaceutical compns., and therapeutic use)

IT Drug delivery systems
(injections; fused uracil derivs. as matrix metalloproteinase inhibitors, pharmaceutical compns., and therapeutic use)

IT Drug delivery systems
(ointments; fused uracil derivs. as matrix metalloproteinase inhibitors, pharmaceutical compns., and therapeutic use)

IT Drug delivery systems
(solns.; fused uracil derivs. as matrix metalloproteinase inhibitors, pharmaceutical compns., and therapeutic use)

IT Drug delivery systems
(suppositories; fused uracil derivs. as matrix metalloproteinase inhibitors, pharmaceutical compns., and therapeutic use)

IT Drug delivery systems
(tablets, coated; fused uracil derivs. as matrix metalloproteinase inhibitors, pharmaceutical compns., and therapeutic use)
IT Drug delivery systems
(tablets; fused uracil derivs. as matrix metalloproteinase inhibitors, pharmaceutical compns., and therapeutic use)
IT 141907-41-7, Matrix metalloproteinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fused uracil derivs. as matrix metalloproteinase inhibitors, pharmaceutical compns., and therapeutic use)
IT 657350-98-6 657350-99-7 657351-00-3 657351-01-4 657351-02-5
657351-03-6 657351-04-7 657351-05-8 657351-06-9 657351-07-0
657351-08-1 657351-09-2 657351-10-5 657351-11-6 657351-12-7
657351-13-8
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fused uracil derivs. as matrix metalloproteinase inhibitors, pharmaceutical compns., and therapeutic use)
IT 169590-42-5, Celecoxib 181695-72-7, Valdecoxib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fused uracil derivs. as matrix metalloproteinase inhibitors, pharmaceutical compns., therapeutic use, and use with other agents)
IT 329900-75-6, Cyclooxygenase 2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; fused uracil derivs. as matrix metalloproteinase inhibitors, pharmaceutical compns., therapeutic use, and use with other agents)
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Ibfb Gmbh; DE 10101324 C 2001 HCAPLUS
(2) Ibfb Gmbh; DE 19940494 C 2001 HCAPLUS
(3) Warner-Lambert Company; WO 02064572 A 2002 HCAPLUS
(4) Warner-Lambert Company; WO 02064598 A 2002 HCAPLUS
(5) Warner-Lambert Company; WO 03033477 A 2003 HCAPLUS
(6) Warner-Lambert Company; WO 03033478 A 2003 HCAPLUS

=> b reg
FILE 'REGISTRY' ENTERED AT 15:46:26 ON 06 JUL 2005
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STRUCTURE FILE UPDATES: 5 JUL 2005 HIGHEST RN 853879-48-8
DICTIONARY FILE UPDATES: 5 JUL 2005 HIGHEST RN 853879-48-8

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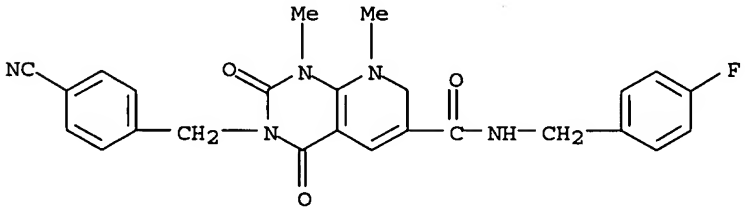
****
* *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *
****

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> d ide l3 tot

L3 ANSWER 1 OF 20 REGISTRY COPYRIGHT 2005 ACS on STN
RN 657351-13-8 REGISTRY
ED Entered STN: 03 Mar 2004
CN Pyrido[2,3-d]pyrimidine-6-carboxamide, 3-[(4-cyanophenyl)methyl]-N-[(4-fluorophenyl)methyl]-1,2,3,4,7,8-hexahydro-1,8-dimethyl-2,4-dioxo- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C25 H22 F N5 O3
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 2 OF 20 REGISTRY COPYRIGHT 2005 ACS on STN
RN 657351-12-7 REGISTRY
ED Entered STN: 03 Mar 2004
CN Pyrido[2,3-d]pyrimidine-6-carboxamide, N-[(4-fluorophenyl)methyl]-1,2,3,4,7,8-hexahydro-1,8-dimethyl-2,4-dioxo-3-(phenylmethyl)- (9CI) (CA INDEX NAME)
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MF C24 H23 F N4 O3
SR CA
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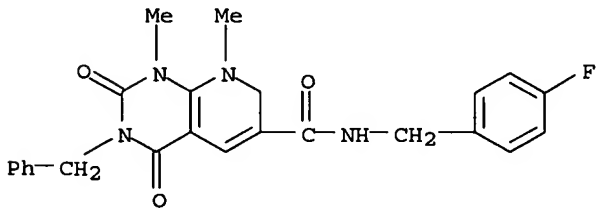

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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 3 OF 20 REGISTRY COPYRIGHT 2005 ACS on STN

RN 657351-11-6 REGISTRY
ED Entered STN: 03 Mar 2004
CN Pyrido[2,3-d]pyrimidine-6-carboxamide, 3-[(3,4-difluorophenyl)methyl]-N-[(4-fluorophenyl)methyl]-1,2,3,4,7,8-hexahydro-1,8-dimethyl-2,4-dioxo- (9CI) (CA INDEX NAME)
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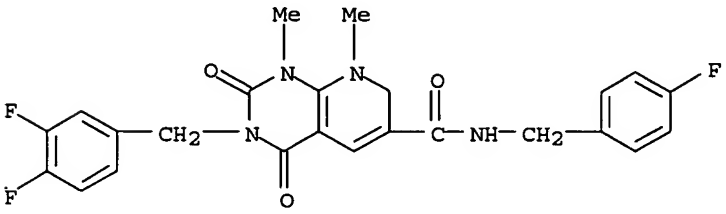
LC STN Files: CA, CAPLUS, USPATFULL



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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 4 OF 20 REGISTRY COPYRIGHT 2005 ACS on STN
RN 657351-10-5 REGISTRY
ED Entered STN: 03 Mar 2004
CN Pyrido[2,3-d]pyrimidine-6-carboxamide, 3-[[4-[[(ethylamino)carbonyl]amino]phenyl]methyl]-1,2,3,4,7,8-hexahydro-N-[(2-methoxy-4-pyridinyl)methyl]-1,8-dimethyl-2,4-dioxo- (9CI) (CA INDEX NAME)
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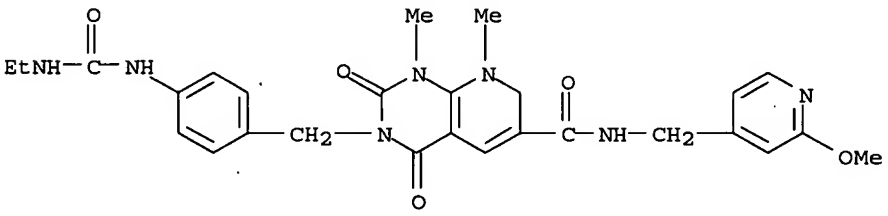

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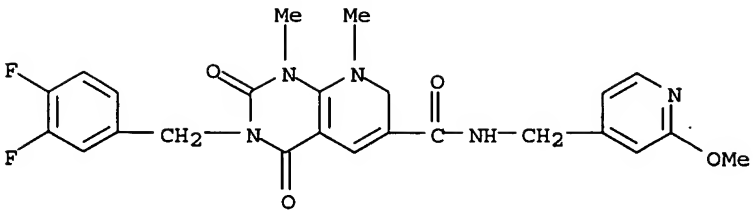
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 5 OF 20 REGISTRY COPYRIGHT 2005 ACS on STN
RN 657351-09-2 REGISTRY
ED Entered STN: 03 Mar 2004
CN Pyrido[2,3-d]pyrimidine-6-carboxamide, 3-[(3,4-difluorophenyl)methyl]-1,2,3,4,7,8-hexahydro-N-[(2-methoxy-4-pyridinyl)methyl]-1,8-dimethyl-2,4-dioxo- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C24 H23 F2 N5 O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 6 OF 20 REGISTRY COPYRIGHT 2005 ACS on STN
RN 657351-08-1 REGISTRY
ED Entered STN: 03 Mar 2004
CN Pyrido[2,3-d]pyrimidine-6-carboxamide, 1,2,3,4,7,8-hexahydro-N-[(2-methoxy-4-pyridinyl)methyl]-1,8-dimethyl-2,4-dioxo-3-(phenylmethyl)- (9CI) (CA INDEX NAME)
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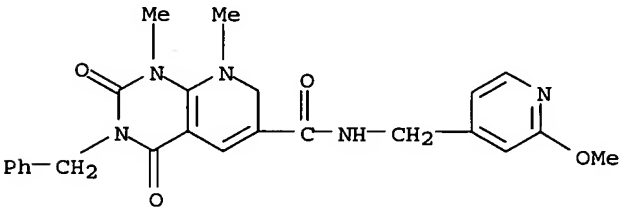
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 7 OF 20 REGISTRY COPYRIGHT 2005 ACS on STN
RN 657351-07-0 REGISTRY
ED Entered STN: 03 Mar 2004
CN Pyrido[2,3-d]pyrimidine-6-carboxamide, 1,2,3,4,7,8-hexahydro-1,8-dimethyl-2,4-dioxo-3-(phenylmethyl)-N-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)
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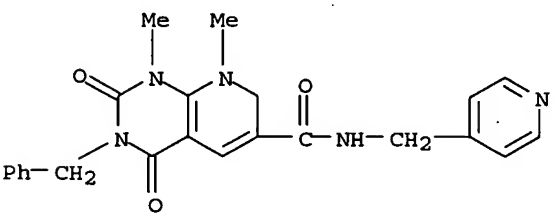
LC STN Files: CA, CAPLUS, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 8 OF 20 REGISTRY COPYRIGHT 2005 ACS on STN
RN 657351-06-9 REGISTRY
ED Entered STN: 03 Mar 2004
CN Pyrido[2,3-d]pyrimidine-6-carboxamide, 3-[(3,4-difluorophenyl)methyl]-1,2,3,4,7,8-hexahydro-1,8-dimethyl-2,4-dioxo-N-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)
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MF C23 H21 F2 N5 O3
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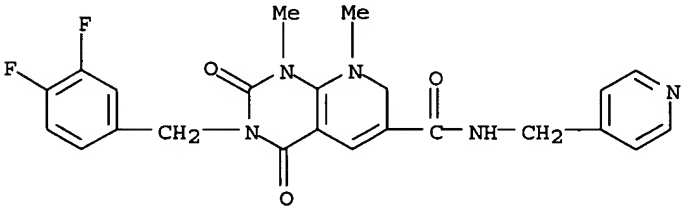

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 9 OF 20 REGISTRY COPYRIGHT 2005 ACS on STN
RN 657351-05-8 REGISTRY
ED Entered STN: 03 Mar 2004
CN Pyrido[2,3-d]pyrimidine-6-carboxamide, 1,2,3,4,7,8-hexahydro-N-[(3-methoxyphenyl)methyl]-1,8-dimethyl-2,4-dioxo-3-(phenylmethyl)- (9CI) (CA INDEX NAME)
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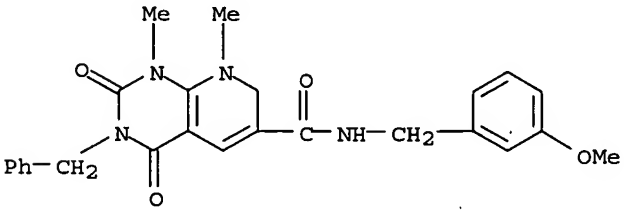

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1 REFERENCES IN FILE CA (1907 TO DATE)
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L3 ANSWER 10 OF 20 REGISTRY COPYRIGHT 2005 ACS on STN
RN 657351-04-7 REGISTRY
ED Entered STN: 03 Mar 2004
CN Pyrido[2,3-d]pyrimidine-6-carboxamide, 3-[(3,5-difluoro-4-

hydroxyphenyl)methyl]-1,2,3,4,7,8-hexahydro-N-[(2-methoxy-4-pyridinyl)methyl]-1,8-dimethyl-2,4-dioxo- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C24 H23 F2 N5 O5
SR CA
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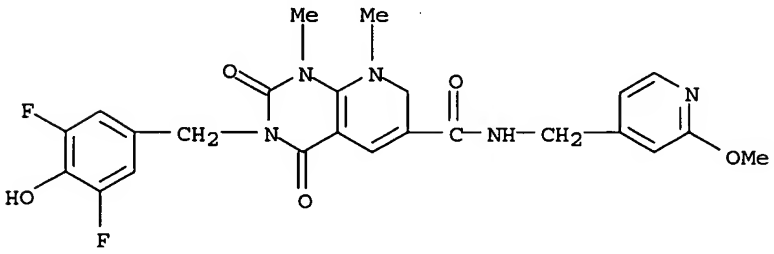

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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 11 OF 20 REGISTRY COPYRIGHT 2005 ACS on STN
RN 657351-03-6 REGISTRY
ED Entered STN: 03 Mar 2004
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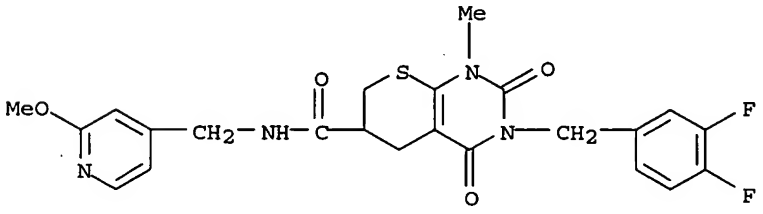

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L3 ANSWER 12 OF 20 REGISTRY COPYRIGHT 2005 ACS on STN
RN 657351-02-5 REGISTRY
ED Entered STN: 03 Mar 2004
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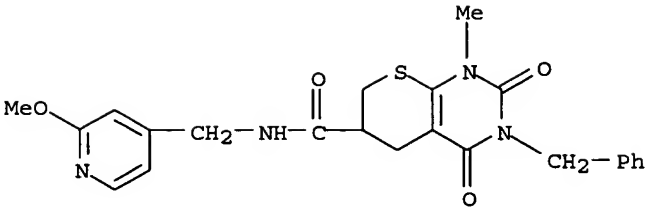

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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L3 ANSWER 13 OF 20 REGISTRY COPYRIGHT 2005 ACS on STN
RN 657351-01-4 REGISTRY
ED Entered STN: 03 Mar 2004
CN 2H-Thiopyrano[2,3-d]pyrimidine-6-carboxamide, 1,3,4,5,6,7-hexahydro-1-methyl-2,4-dioxo-3-(phenylmethyl)-N-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)
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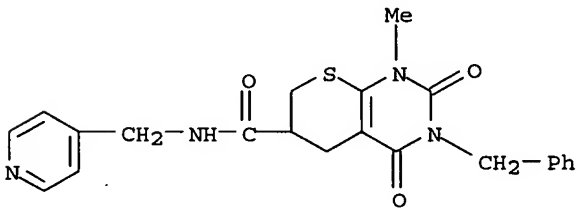
LC STN Files: CA, CAPLUS, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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L3 ANSWER 14 OF 20 REGISTRY COPYRIGHT 2005 ACS on STN
RN 657351-00-3 REGISTRY
ED Entered STN: 03 Mar 2004
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FS 3D CONCORD
MF C22 H20 F2 N4 O3 S
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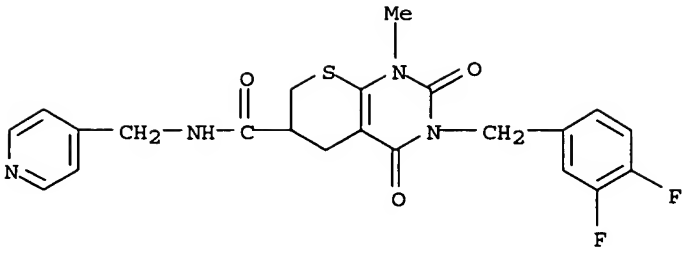
LC STN Files: CA, CAPLUS, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 15 OF 20 REGISTRY COPYRIGHT 2005 ACS on STN
RN 657350-99-7 REGISTRY
ED Entered STN: 03 Mar 2004
CN 2H-Thiopyrano[2,3-d]pyrimidine-6-carboxamide, 1,3,4,5,6,7-hexahydro-N-[(3-methoxyphenyl)methyl]-1-methyl-2,4-dioxo-3-(phenylmethyl)- (9CI) (CA INDEX NAME)
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MF C24 H25 N3 O4 S
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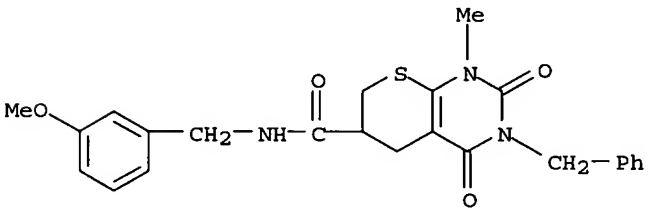
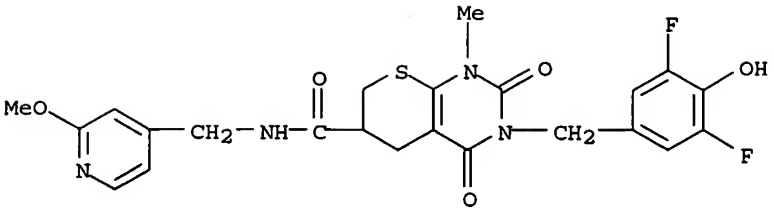


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 16 OF 20 REGISTRY COPYRIGHT 2005 ACS on STN
RN 657350-98-6 REGISTRY
ED Entered STN: 03 Mar 2004
CN 2H-Thiopyrano[2,3-d]pyrimidine-6-carboxamide, 3-[(3,5-difluoro-4-hydroxyphenyl)methyl]-1,3,4,5,6,7-hexahydro-N-[(2-methoxy-4-pyridinyl)methyl]-1-methyl-2,4-dioxo- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C23 H22 F2 N4 O5 S
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

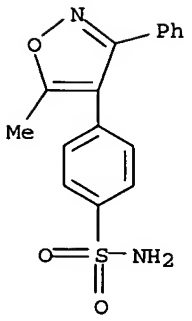
L3 ANSWER 17 OF 20 REGISTRY COPYRIGHT 2005 ACS on STN
RN 329900-75-6 REGISTRY
ED Entered STN: 04 Apr 2001
CN Synthetase, prostaglandin endoperoxide, 2 (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Arachidonate cyclooxygenase 2
CN COX-2
CN Cyclooxygenase 2
CN Cyclooxygenase II
CN Prostaglandin endoperoxidase synthase 2
CN Prostaglandin endoperoxide H synthase-2
CN Prostaglandin endoperoxide synthase-2
CN Prostaglandin endoperoxide synthetase 2
CN Prostaglandin G/H synthase-2
CN Prostaglandin H synthase-2
MF Unspecified
CI MAN
SR CA
LC STN Files: BIOSIS, CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

6798 REFERENCES IN FILE CA (1907 TO DATE)
7 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
6841 REFERENCES IN FILE CAPLUS (1907 TO DATE)

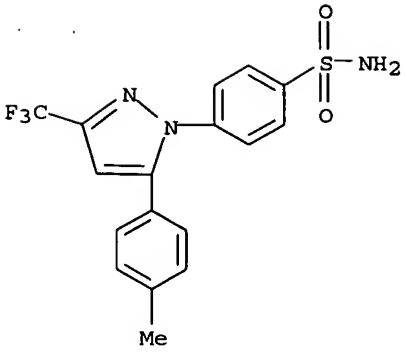
L3 ANSWER 18 OF 20 REGISTRY COPYRIGHT 2005 ACS on STN
RN 181695-72-7 REGISTRY
ED Entered STN: 10 Oct 1996
CN Benzenesulfonamide, 4-(5-methyl-3-phenyl-4-isoxazolyl)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 4-(5-Methyl-3-phenylisoxazol-4-yl)benzenesulfonamide
CN Bextra
CN SC 65872
CN Valdecoxib
FS 3D CONCORD
MF C16 H14 N2 O3 S
CI COM
SR CA
LC STN Files: ADISINSIGHT, ANABSTR, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MRCK*, PATDPASPC, PHAR, PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

431 REFERENCES IN FILE CA (1907 TO DATE)
21 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
433 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 19 OF 20 REGISTRY COPYRIGHT 2005 ACS on STN
RN **169590-42-5** REGISTRY
ED Entered STN: 02 Nov 1995
CN Benzenesulfonamide, 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 4-[5-(4-Methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide
CN Celebrex
CN Celecoxib
CN Celocoxib
CN SC 58635
CN YM 177
FS 3D CONCORD
DR 184007-95-2, 194044-54-7
MF C17 H14 F3 N3 O2 S
CI COM
SR US Adopted Names Council (USAN)
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, HSDB*, IMSCOSEARCH, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, MSDS-OHS, PATDPASPC, PHAR, PROMT, PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1469 REFERENCES IN FILE CA (1907 TO DATE)
39 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1480 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 20 OF 20 REGISTRY COPYRIGHT 2005 ACS on STN
RN 141907-41-7 REGISTRY
ED Entered STN: 19 Jun 1992
CN Proteinase, matrix metallo- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Matrix metalloendoproteinase
CN Matrix metalloprotease
CN Matrix metalloprotease HIPHUM35
CN Matrix metalloproteinase
CN Matrix-degrading metalloproteinase
CN Matrixin
MF Unspecified
CI MAN
SR CA
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, CA, CAPLUS, CEN, CIN, PROMT, TOXCENTER, USPAT2, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3395 REFERENCES IN FILE CA (1907 TO DATE)
17 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
3410 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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FILE 'WPIX' ENTERED AT 15:46:34 ON 06 JUL 2005
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FILE LAST UPDATED: 04 JUL 2005 <20050704/UP>
MOST RECENT DERWENT UPDATE: 200542 <200542/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

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=> d iall dcn tot l4

L4 ANSWER 1 OF 1 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-238726 [22] WPIX
DOC. NO. CPI: C2004-093387
TITLE: New 5,6-fused uracil derivatives are matrix metalloproteinase inhibitors useful to treat arthritis, heart disease, asthma, age-related macular degeneration, psoriasis and periodontal disease.
DERWENT CLASS: B02
INVENTOR(S): ROARK, W H
PATENT ASSIGNEE(S): (WARN) WARNER LAMBERT CO LLC; (ROAR-I) ROARK W H
COUNTRY COUNT: 103
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2004014921	A1	20040219	(200422)*	EN	193	C07D495-04
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW						
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW						
AU 2003250465	A1	20040225	(200456)			C07D495-04
US 2004224951	A1	20041111	(200475)			A61K031-519<--

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE	
WO 2004014921	A1	WO 2003-IB3505	20030804	
AU 2003250465	A1	AU 2003-250465	20030804	
US 2004224951	A1 Provisional	US 2002-403037P	20020813	<--
		US 2003-634489	20030805	

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003250465	A1 Based on	WO 2004014921

PRIORITY APPLN. INFO: US 2002-403037P 20020813; US 2003-634489 20030805
INT. PATENT CLASSIF.:
MAIN: A61K031-519; C07D495-04
SECONDARY: A61K031-53; A61P019-02; C07D471-04; C07D487-02
BASIC ABSTRACT:
WO2004014921 A UPAB: 20040331
NOVELTY - 5,6-fused uracil derivatives (I) and their salts are new.
DETAILED DESCRIPTION - 5,6-fused uracil derivatives of formula (I)

and their salts are new.

R1 = C5 or C6 cycloalkyl-(1-8C alkylenyl), substituted C5 or C6 cycloalkyl-(1-8C alkylenyl), 8-10C bicycloalkyl-(1-8C alkylenyl), substituted 8-10C bicycloalkyl-(1-8C alkylenyl), 5 or 6 membered heterocycloalkyl-(1-8C alkylenyl), substituted 5 or 6 membered heterocycloalkyl-(1-8C alkylenyl), 8- 10- membered heterobicycloalkyl-(1-8C alkylenyl), substituted 8- 10-membered heterobicycloalkyl-(1-8C alkylenyl), phenyl-(1-8C alkylenyl), substituted phenyl-(1-8C alkylenyl), naphthyl-(1-8C alkylenyl), substituted naphthyl-(1-8C alkylenyl), 5 or 6 membered heteroaryl-(1-8C alkylenyl), substituted 5 or 6 membered heteroaryl-(1-8C alkylenyl), 8- 10-membered heterobiaryl-(1-8C alkylenyl), substituted 8- 10-membered heterobiaryl-(1-8C alkylenyl), phenyl, substituted phenyl, naphthyl, substituted naphthyl, 5 or 6 membered heteroaryl, substituted 5 or 6 membered heteroaryl, 8- 10-membered heterobiaryl or substituted 8- 10-membered heterobiaryl;

R2 = H, 1-6C alkyl, phenyl-(1-8C alkylenyl), substituted phenyl-(1-8C alkylenyl), naphthyl-(1-8C alkylenyl), substituted naphthyl-(1-8C alkylenyl), 5 or 6 membered heteroaryl-(1-8C alkylenyl), substituted 5 or 6 membered heteroaryl-(1-8C alkylenyl), 8- 10-membered heterobiaryl-(1-8C alkylenyl), substituted 8- 10-membered heterobiaryl-(1-8C alkylenyl), phenyl-O-(1-8C alkylenyl), substituted phenyl-O-(1-8C alkylenyl), phenyl-S-(1-8C alkylenyl), substituted phenyl-S-(1-8C alkylenyl), phenyl-S(O)-(1-8C alkylenyl), substituted phenyl-S(O)-(1-8C alkylenyl), phenyl-S(O)2-(1-8C alkylenyl) or substituted phenyl-S(O)2-(1-8C alkylenyl) (each substituted R1 and R2 contains from 1 to 4 substituents, each independently on a carbon or nitrogen atom of 1-6C alkyl, CN, CF3, HO, (1-6C alkyl)-O, (1-6C alkyl)-S(O)2, H2N, (1-6C alkyl)-N(H), (1-6C alkyl)2-N, (1-6C alkyl)-C(O)O-(1-8C alkylenyl)m, (1-6C alkyl)-C(O)O-(1- 8-membered heteroalkylenyl)m, (1-6C alkyl)-C(O)N(H)-(1-8C alkylenyl)m, (1-6C alkyl)-C(O)N(H)-(1- to 8-membered heteroalkylenyl)m, H2NS(O)2-(1-8C alkylenyl), (1-6C alkyl)-N(H)S(O)2-(1-8C alkylenyl)m, (1-6C alkyl)2-NS(O)2-(1-8C alkylenyl)m, 3- 6-membered heterocycloalkyl-(G)m, substituted 3- 6-membered heterocycloalkyl-(G)m, 5 or 6 membered heteroaryl-(G)m, substituted 5 or 6 membered heteroaryl-(G)m, (1-6C alkyl)-S(O)2-N(H)-C(O)-(1-8C alkylenyl)m or (1-6C alkyl)-C(O)-N(H)-S(O)2-(1-8C alkylenyl)m (wherein each substituent on a carbon atom of Halo or HO2C, wherein 2 substituents may be taken together with a carbon atom to which they are both bonded to form the group C=O, wherein two adjacent, substantially sp2 carbon atoms may be taken together with a diradical substituent to form a cyclic diradical of formula (1-14));

R = H or 1-6C alkyl;

G = CH2, O, S, S(O) or S(O)2;

m = 0 or 1;

R7 = H, CH3, CH3O, CH=CH2, HO, CF3, CN, HC(O), CH3C(O), HC(NOH), H2N, (CH3)-N(H), (CH3)2-N, H2NC(O), (CH3)-N(H)C(O), (CH3)2-NC(O), halo or CO2H;

Y5, Y8 = CH2, C(O), O, S, S(O), S(O)2 or N(R5); or CR7+Y8 = -C=CH- or -C=N-

Y6 = CH2 or C(O); or CY6+R7 = -HC=C (wherein R7 is not simultaneously taken together with Y6 and Y8);

R4, R5 = H, CH3, CH3O, CH=CH2, HO, CF3, CN, HC(O), CH3C(O), HC(NOH), H2N, (CH3)-N(H), (CH3)2-N, H2NC(O), (CH3)-N(H)C(O) or (CH3)2-NC(O);

Q = OC(O), CH(R6)C(O), OC(NR6), CH(R6)C(NR6), N(R6)C(O), N(R6)C(S), N(R6)C(NR6), N(R6)CH2, SC(O), CH(R6)C(S), SC(NR6), trans-(H)C=C(H), cis-(H)C=C(H), C triple bond C, CH2C triple bond C, C triple bond CCH2, CF2C triple bond C or C triple bond CCF2 or formula (a-g);

R6 = H, 1-6C alkyl, 3-6C cycloalkyl, 3- 6-membered heterocycloalkyl, phenyl, benzyl or 5 or 6 membered heteroaryl;

X = O, S, N(H) or N(1-6C alkyl); and

V = C(H) or N.

Where each 8-10C bicycloalkyl is a bicyclic carbocyclic ring that contains 8, 9 or 10 member carbon atoms which are 5,5-fused, 6,5-fused or 6,6-fused bicyclic rings, respectively and the ring is saturated or optionally contains one carbon-carbon double bond (each of 8-10-membered heterobicycloalkyl is a bicyclic ring that contains carbon atoms and from 1-4 heteroatoms of 2 O , 1 S, 1 S(O), 1 S(O)2,1 N, 4 N(H) or 4 N(1-6C

alkyl) and when two O atoms or one O atom and one S atom are present, the two O atoms or one O atom and one S atom are not bonded to each other) and the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double bond and the heterobicycloalkyl is a 5,5-fused, 6,5-fused, or 6,6-fused bicyclic ring, respectively, each heterocycloalkyl is a ring that contains carbon atoms and from 1-4 heteroatoms of 2 O , 1 S, 1 S(O), 1 S(O)2,1 N, 4 N(H) or 4 N(1-6C alkyl) and when two O atoms or one O atom and one S atom are present the two O atoms or one O atom and one S atom are not bonded to each other and the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double bond, each 5-membered heteroaryl contains carbon atoms and from 1 to 4 heteroatoms of 1 O , 1 S, 1 N(H), 1 N(1-6C alkyl) or 4 N, and each 6-membered heteroaryl contains carbon atoms and 1 or 2 heteroatoms of N, N(H) or N(1-6C alkyl) or 5- and 6-membered heteroaryl are monocyclic rings, each heterobiaryl contains carbon atoms and from 1 to 4 heteroatoms of 1 O, 1 S, 1 N(H), 1 N(1-6C alkyl) or 4 N and the 8-, 9-, and 10-membered heterobiaryl are 5,5-fused, 6,5-fused, and 6,6-fused bicyclic rings, respectively, and at least 1 of the 2 fused rings of a bicyclic ring is aromatic, where when the O and S atoms both are present, the O and S atoms are not bonded to each other, where with any (1-6C alkyl)2-N group, the 1-6C alkyl groups may be optionally taken together with the nitrogen atom to which they are attached to form a 5- or 6-membered heterocycloalkyl.

ACTIVITY - Antiarthritic; Cardiant; Neuroprotective; Antirheumatic; Ophthalmological; Respiratory-Gen.; Antiasthmatic; Antiinflammatory; Osteopathic; Antipsoriatic.

MECHANISM OF ACTION - Matrix metalloproteinase (MMP) inhibitor.

USE - (I) are used to treat arthritis (claimed). (I) are also used to treat diseases resulting from MMP-mediated tissue break down e.g. heart disease, multiple sclerosis, rheumatoid arthritis, age-related macular degeneration, chronic obstructive pulmonary disease, asthma, periodontal diseases, psoriasis, atherosclerosis and osteoporosis.

ADVANTAGE - (I) is nontoxic, their preparation is easy, well-tolerated and their topical or oral administration is easy. (I) were tested for their ability to inhibit matrix metalloprotienase (MMP)-13. The results show that (I) are potent inhibitor of MMP enzymes and useful to treat diseases mediated by the MMP enzymes.

Dwg.0/0

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; GI; DCN
MANUAL CODES: CPI: B06-H; B14-C09; B14-F01; B14-F07; B14-K01; B14-N01; B14-N03; B14-N06B; B14-N17C; B14-S01

M2 *01* DCN: RADLD5-T; RADLD5-N
M2 *02* DCN: RADLD4-T; RADLD4-N
M2 *03* DCN: RADLD2-T; RADLD2-N
M2 *04* DCN: RADLD0-T; RADLD0-N
M2 *05* DCN: RADLCY-T; RADLCY-N
M2 *06* DCN: RADLCW-T; RADLCW-N
M2 *07* DCN: RADLCV-T; RADLCV-N
M2 *08* DCN: RADLCU-T; RADLCU-N
M2 *09* DCN: RADLCT-T; RADLCT-N
M2 *10* DCN: RADLBU-T; RADLBU-N
M2 *11* DCN: RADLBM-T; RADLBM-N
M2 *12* DCN: RADLBE-T; RADLBE-N
M2 *13* DCN: RADLAM-T; RADLAM-N
M2 *14* DCN: RADLAG-T; RADLAG-N
M2 *15* DCN: RADLA5-T; RADLA5-N
M2 *16* DCN: RADL9S-T; RADL9S-N
M2 *17* DCN: 0125-46301-T; 0125-46301-N
M2 *18* DCN: 0125-46305-T; 0125-46305-N
M2 *19* DCN: 0125-46304-T; 0125-46304-N

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